

**Paramagnetic fluorinated nanoemulsions for sensitive cellular fluorine-19 magnetic resonance imaging.**

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**Public Summary:**

Fluorine-19 magnetic resonance imaging (19F MRI) probes enable quantitative in vivo detection of cell therapies and inflammatory cells. Here, we describe the formulation of perfluorocarbon-based nanoemulsions with improved sensitivity for cellular MRI. Reduction of the 19F spin-lattice relaxation time (T1) enables rapid imaging and an improved signal-to-noise ratio, thereby improving cell detection sensitivity. We synthesized metal-binding beta-diketones conjugated to linear perfluoropolyether (PFPE), formulated these fluorinated ligands as aqueous nanoemulsions, and then metallated them with various transition and lanthanide ions in the fluorous phase. Iron(III) tris-beta-diketonate ('FETRIS') nanoemulsions with PFPE have low cytotoxicity (<20%) and superior MRI properties. Moreover, the 19F T1 can readily be reduced by an order of magnitude and tuned by stoichiometric modulation of the iron concentration. The resulting 19F MRI detection sensitivity is enhanced by three- to fivefold over previously used tracers at 11.7 T, and is predicted to increase by at least eightfold at the clinical field strength of 3 T.

**Scientific Abstract:**

Fluorine-19 magnetic resonance imaging (19F MRI) probes enable quantitative in vivo detection of cell therapies and inflammatory cells. Here, we describe the formulation of perfluorocarbon-based nanoemulsions with improved sensitivity for cellular MRI. Reduction of the 19F spin-lattice relaxation time (T1) enables rapid imaging and an improved signal-to-noise ratio, thereby improving cell detection sensitivity. We synthesized metal-binding beta-diketones conjugated to linear perfluoropolyether (PFPE), formulated these fluorinated ligands as aqueous nanoemulsions, and then metallated them with various transition and lanthanide ions in the fluorous phase. Iron(III) tris-beta-diketonate ('FETRIS') nanoemulsions with PFPE have low cytotoxicity (<20%) and superior MRI properties. Moreover, the 19F T1 can readily be reduced by an order of magnitude and tuned by stoichiometric modulation of the iron concentration. The resulting 19F MRI detection sensitivity is enhanced by three- to fivefold over previously used tracers at 11.7 T, and is predicted to increase by at least eightfold at the clinical field strength of 3 T.

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